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## Diet quality and breast cancer incidence in the Multiethnic Cohort

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### Abstract

This study investigated the relation of diet quality indexes (DQI) with breast cancer incidence among women from the Multiethnic Cohort (MEC). Participants completed a questionnaire with a validated food frequency questionnaire. Scores for Healthy Eating Index 2015 (HEI-2015), Alternate Healthy Eating Index 2010 (AHEI-2010), alternate Mediterranean diet score (aMED), and Dietary Approaches to Stop Hypertension (DASH) were divided into quintiles (Q1-Q5). Cox regression was applied to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for DQIs and breast cancer risk adjusted for known risk factors. The respective HRs for Q5 vs. Q1 were: 1.06 (95% CI, 0.98-1.14) for HEI-2015, 0.96 (95% CI, 0.90-1.04) for AHEI-2010, 1.01 (95% CI, 0.94-1.09) for aMED, and 0.95 (95% CI, 0.88-1.02) for DASH ( $p_{\text{trend}} > 0.05$  for all). However, overweight and obesity were significantly associated with breast cancer incidence. Despite the null association for DQIs, diet quality may lower breast cancer risk through its positive influence on weight status.

### Keywords

Diet quality; breast cancer incidence; ethnicity; nutrition; cohort

### Introduction

Breast cancer is the most common cancer among women in the United States and annual incidence rates continue to rise. It is well known that a higher body mass index (BMI) increases risk for breast cancer among postmenopausal women,<sup>1</sup> but it is unclear whether diet quality also contributes. Four diet quality indexes (DQIs) have been developed using an *a priori* approach to assess adherence to specific recommendations: Healthy Eating Index 2015 (HEI-2015), Alternate Healthy Eating Index 2010 (AHEI-2010), alternate Mediterranean diet score (aMED), and the Dietary Approaches to Stop Hypertension score

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Conflict of Interest

All authors declare no conflict of interest in this research study.

(DASH).<sup>2</sup> Although all DQIs represent adherence to a high quality diet, we were interested in their potential differences given the variety of nutritional patterns across populations.

Higher DQIs have been associated with reduced risk of mortality, diabetes, colorectal cancer, and cardiovascular disease.<sup>3</sup> The association between DQIs and breast cancer incidence is still unclear.<sup>4</sup> Some previous studies have suggested a reduced risk for postmenopausal breast cancer associated with DQIs, mainly the Mediterranean diet,<sup>4</sup> however, other studies in post-menopausal women assessing DASH, HEI, and AHEI had null findings.<sup>4</sup> As previous analyses within the Multiethnic Cohort (MEC) found an inverse association of diet quality with cancer mortality and colorectal cancer incidence,<sup>5,6</sup> the purpose of the current analysis was to evaluate any relation between *a priori* DQIs and breast cancer incidence within the ethnically diverse MEC.

## Methods

The study population was derived from the prospective MEC study, a prospective follow-up study of more than 200,000 adults living in Hawaii or the Los Angeles area who were recruited at ages 45-75 from 1993-1996 and followed until 2014.<sup>5,7</sup> Identification of breast cancer cases through cancer registries has been previously described.<sup>7</sup> For the current analysis, women from five major ethnic groups (African American, Native Hawaiian, Japanese American, Latino, and white) and free of breast cancer at cohort entry were included (Table 1). Women from ethnic groups other than the five main groups (N=8,046), with pre-existing breast cancer (N=5,025), invalid dietary information (N=4,394) due to incomplete reporting, or inconsistent dates (N=2) were excluded. The final dataset included 101,291 women, of whom 7,749 were diagnosed with *in situ* or invasive breast cancer over the study period. The Institutional Review Boards at the University of Hawaii and the University of Southern California approved the study protocol.

Participants completed a self-administered, validated quantitative food frequency questionnaire including more than 180 food items.<sup>8</sup> Although no true validation study was performed, a calibration sub-study found acceptable correlations between the FFQ and three 24-hour dietary recalls among 1,606 cohort members; mean correlations ranged from 0.57-0.74 for nutrient densities. Detailed information on the calculation of the HEI-2015, AHEI-2010, aMED, and DASH as assessed at cohort entry was previously published.<sup>5</sup> Total scores of the 4 DQIs were categorized into quintiles for analysis based on the distribution of the study dataset.

Cox regression with age as the time-metric and ethnicity as strata was applied to examine the association between diet quality and breast cancer incidence censoring at breast cancer diagnosis, death, or end of 2014. Separate models were fit for each of the four DQIs. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated for each DQI quintile using the lowest quintile as reference category and for BMI categories using normal weight (BMI 20 to <25) as reference category. All models were adjusted for covariates known to have association with breast cancer (Table 2). All missing values for covariates were coded as a separate category. Tests for trend were based on the DQIs scores as continuous variables. For sensitivity analyses, the DQIs were modeled excluding women with missing

BMI values (N=1,370 missing), including only women with latency follow up period of 3 or more years (N=97,980), women with estrogen/progesterone positive breast cancer (N=4,079 cases), or women with estrogen/progesterone negative breast cancer (N=999 cases).

## Results

Among 101,291 women in the MEC sample, 7,749 were diagnosed with breast cancer during 17.4±5.6 mean years of follow-up. 112 women were diagnosed at or younger than 50 years of age and 7,637 were diagnosed older than 50 years. Only 13,991 women were premenopausal. The proportion of women diagnosed with breast cancer was highest for Native Hawaiians (10.2%) (Table 1). Across all indexes, women with the highest diet quality (Q5) tended to be white, older, were never or former smokers, and more physical activity than women with the lowest diet quality (Q1). Women with the lowest diet quality (Q1) had the highest BMIs.

Comparing the highest to the lowest quintile, no association with breast cancer risk was observed for any of the four DQIs. In general, HRs for all DQIs remained close to one, ranging from 0.91 to 1.11 (Table 2). Only for the HEI-2015, the HRs for the Q3 and Q4 were elevated. Trend analysis for all DQIs did not indicate significance (all  $P_{\text{trend}} > 0.05$ ). Tests for heterogeneity did not show statistically significant differences across the 5 ethnic groups (all  $P_{\text{heterogeneity}} > 0.05$ ). Sensitivity analyses that excluded women with missing BMI, included only women with latency follow up period of 3 or more years, included only women with estrogen/progesterone positive breast cancer or estrogen/progesterone negative breast cancer also showed null associations between the 4 DQIs and breast cancer risk (data not shown).

In contrast, overweight and obesity were associated with an elevated breast cancer incidence in models for all for DQIs (data not shown). For example, the HRs were 1.19 (95% CI, 1.12-1.25) and 1.32 (95% CI, 1.23-1.41) for overweight (BMI 25 to <30) and obese (BMI 30) women, respectively, in the HEI-2015 models.

## Discussion

In this multiethnic cohort of 101,291 women, 4 different DQIs did not predict breast cancer incidence; the elevated HRs for two quintiles of the HEI-2015 may be a chance finding. These null associations between diet quality and breast cancer incidence are inconsistent with several published research,<sup>4</sup> however, other studies observed mixed findings for several DQIs. Two out of 5 studies reviewed by the World Cancer Research Fund (WCRF) that assessed the Mediterranean diet score and postmenopausal breast cancer incidence results had inverse significant associations.<sup>4</sup> Only 4 out of 17 studies assessing other DQIs detected a significant inverse association in postmenopausal breast cancer.<sup>4</sup> These discrepancies should be interpreted with caution as dietary assessment and calculation methods of diet quality index scores differed considerably across studies.<sup>4,9-11</sup>

Although other studies have reported null associations between DQIs and breast cancer among premenopausal women, we did not see an association among a diverse cohort with mostly postmenopausal women.<sup>9</sup> Separate models for pre- and postmenopausal women were

not applied in our study as the number of premenopausal cases was small. Results from a recent case-control study indicate a reduced breast cancer risk with adherence to the Mediterranean diet score without differences in pre- and postmenopausal women.<sup>10</sup> Other studies have reported an increased risk in breast cancer associated with *a posteriori* dietary patterns including lower quality diets such as the Western diet and reduced risk in breast cancer with the Mediterranean diet or other prudent diets.<sup>11</sup> On the other hand, several studies reviewed by the WCRF did not show significant associations between diet quality and breast cancer incidence.<sup>4</sup> According to the WCRF, obesity appears to be the major nutritional risk factor for breast cancer.<sup>4</sup> At the same time, there is evidence that a high quality diet is associated with a lower likelihood of excess body weight<sup>12</sup> as also seen in Table 1 and that overweight or obese women have a higher breast cancer incidence.

Our study had several limitations. No data on fat mass and energy balance were collected in this large cohort. In addition, only nutritional data from the FFQ at cohort entry were analyzed. Thus, the impact of changes in diet quality over time could not be assessed.

## Conclusion

Our null findings contribute to the overall evidence on the relationship between diet quality and breast cancer risk among diverse ethnic groups. Although diet quality was not directly associated with breast cancer incidence, nutrition remains important in breast cancer prevention as obesity, a strong modifiable risk factor for postmenopausal breast cancer, is influenced by diet quality.<sup>4</sup>

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**Table 1.**

Characteristics of 101,291 Women by Lowest (Q1) and Highest (Q5) Quintile of Diet Quality

	HEI-2015		AHEI-2010		aMED		DASH	
	Q1	Q5	Q1	Q5	Q1	Q5	Q1	Q5
<b>Mean score (points)</b>	53.8 (5.1)	83.0 (3.7)	52.0 (4.4)	77.8 (4.0)	1.6 (0.6)	6.5 (0.7)	18 (1.9)	29.9 (1.9)
<b>Age at cohort entry (yrs)</b>	57.5 (8.7)	62.5 (8.4)	58.0 (8.8)	61.6 (8.7)	59.0 (8.9)	61.1 (8.7)	57.5 (8.7)	62.1 (8.5)
<b>Ethnicity<sup>*</sup>, %</b>								
White	16.1	24.8	19.8	22.6	22.6	23.1	13.9	30.3
African American	15.5	25.9	21.8	17.9	22.3	23.5	25.4	19.0
Native Hawaiian	25.8	16.6	21.0	19.7	18.4	29.2	30.8	17.7
Japanese American	20.8	18.5	15.1	26.7	18.3	26.4	26.2	19.0
Latina	25.5	12.4	24.4	10.9	23.6	19.0	19.0	23.2
<b>Body mass index, kg/m<sup>2</sup><sup>*</sup>, %</b>								
<20	19.2	24.4	16.6	27.5	19.8	26.6	19.0	28.1
20 to <25	17.9	22.5	17.8	23.1	19.9	25.2	20.0	25.2
25 to <30	19.7	19.4	20.5	17.9	21.8	22.8	21.9	21.3
30	24.3	15.2	24.3	15.3	23.2	21.1	25.9	17.7
<b>Smoking status<sup>*</sup>, %</b>								
Never	18.0	21.1	18.4	20.6	19.9	25.0	19.5	24.1
Former	17.3	22.5	17.8	22.7	20.2	24.7	19.3	24.4
Current	33.2	11.2	30.8	12.9	29.3	16.4	37.0	12.0
<b>Alcohol intake<sup>*</sup>, g, %</b>								
<1 per month	21.0	19.8	21.2	18.2	22.6	21.9	22.4	22.1
<1 per day	18.8	20.2	16.5	22.9	17.5	29.0	20.3	23.8
1 to 2 per day	15.6	22.6	7.5	40.0	20.5	24.5	20.3	23.5
>2 per day	17.4	19.9	37.0	9.2	25.3	18.8	24.9	19.2
<b>Physical activity<sup>*</sup>, min/day, %</b>								
<30	23.8	16.0	23.3	16.1	24.7	19.7	25.8	18.4
30	16.9	23.3	17.4	23.2	18.5	26.9	18.9	25.6
<b>Educational status<sup>*</sup>, years, %</b>								
12	23.2	16.3	22.1	17.0	22.8	21.8	24.1	20.0
13–15	18.7	21.3	19.6	20.6	21.4	23.6	22.1	22.1
16	15.1	25.8	16.3	25.4	18.1	27.3	17.2	28.0
<b>Family history<sup>*</sup>, %</b>	18.2	21.4	18.7	21.0	21.2	24.7	19.8	23.6
<b>Age at menarche<sup>*</sup>, years, %</b>								
<12	19.9	20.2	20.6	19.9	21.7	23.2	22.4	22.0
13-14	19.4	20.6	19.2	20.1	20.8	24.1	21.0	23.1
15	21.6	17.9	19.7	20.2	20.5	24.1	22.2	22.9
<b>Parity<sup>*</sup>, %</b>								
0	17.5	24.2	18.7	23.8	20.0	25.3	19.0	26.4
1	18.5	21.6	19.5	21.0	21.2	24.4	21.3	23.3

	HEI-2015		AHEI-2010		aMED		DASH	
	Q1	Q5	Q1	Q5	Q1	Q5	Q1	Q5
2 to 3	19.5	20.5	19.4	21.1	21.3	23.4	22.4	22.1
4	22.2	17.1	21.5	16.7	21.7	23.1	22.6	21.1
<b>Age at menopause<sup>*</sup>, years, %</b>								
Premenopause	29.8	12.4	27.1	15.7	25.6	19.6	32.8	15.2
<45	19.8	20.0	20.9	18.7	22.0	22.5	21.9	21.7
45-49	19.4	20.9	19.7	20.5	20.9	24.4	20.4	23.7
50	15.7	23.5	16.0	23.2	18.2	26.3	17.4	26.1
<b>Hormone use<sup>*</sup>, %</b>								
Never used	23.0	17.4	22.3	18.1	22.6	22.2	25.1	19.9
Previously used estrogen only	17.1	22.8	18.5	21.3	20.0	25.5	18.9	25.0
Currently use estrogen only	16.2	24.2	17.3	22.3	19.9	24.9	18.4	25.0
Currently use or have used estrogen w/ progesterone	15.5	23.5	16.1	23.7	19.1	25.9	17.4	26.7

\* Row percents presented.

Abbreviations: HEI-2015 = Healthy eating Index 2015; AHEI-2010 = Alternate Healthy Eating Index 2010; aMED = Alternate Mediterranean Diet; DASH = Dietary Approaches to Stop Hypertension.

**Table 2.**

Risk for Breast Cancer by Quintiles of Dietary Index Scores among Women (N=101,291) in the Multiethnic Cohort Study

Diet Quality Index	Quintile Range	Cases	Person-Years of Follow-up	HR (95% CI) <sup>a</sup>
<b>HEI-2015<sup>b</sup></b>				
1	(23.5-60.0)	1,387	355,124	1.00 (ref)
2	(60.0-66.4)	1,507	353,775	1.06 (0.99-1.14)
3	(66.4-72.0)	1,578	351,276	1.09 (1.02- 1.18)
4	(72.0-78.1)	1,677	351,029	1.13 (1.05-1.22)
5	(78.1-99.8)	1,600	351,056	1.06 (0.98-1.14)
P for trend <sup>c</sup>				0.07
<b>AHEI-2010</b>				
1	(28.7-57.3)	1,491	352,464	1.00 (ref)
2	(57.3-62.8)	1,449	351,807	0.95 (0.88-1.02)
3	(62.8-67.4)	1,567	351,194	1.00 (0.93-1.08)
4	(67.4-72.9)	1,631	352,652	1.01 (0.94-1.09)
5	(72.9-100.9)	1,611	354,187	0.96 (0.90-1.04)
P for trend <sup>c</sup>				0.49
<b>aMED</b>				
1	(0-2)	1,569	370,907	1.00 (ref)
2	3	1,364	318,598	1.00 (0.93-1.07)
3	4	1,519	337,155	1.03 (0.96-1.11)
4	5	1,394	317,695	1.00 (0.92-1.08)
5	(6-9)	1,903	417,948	1.01 (0.94-1.09)
P for trend <sup>c</sup>				0.72
<b>DASH<sup>b</sup></b>				
1	(9-20)	1,735	386,987	1.00 (ref)
2	(21-22)	1,060	258,448	0.91 (0.84-0.98)
3	(23-25)	2,015	444,494	1.00 (0.94-1.07)
4	(26-27)	1,221	275,457	0.97 (0.90-1.05)
5	(28-39)	1,718	396,918	0.95 (0.88-1.02)
P for trend <sup>c</sup>				0.38

<sup>a</sup>Hazard ratios and 95% CIs obtained by Cox regression with age as the time-metric and adjusted for age, total energy intake, BMI, smoking status, physical activity, education, age at menarche, age at first live birth, parity, age at menopause, family history of breast cancer, estrogen and progestin use, diet quality index depending on the model.

<sup>b</sup>HEI-2015 and DASH models also adjusted for alcohol intake as they did not include an alcohol component in their scores.

<sup>c</sup>p-values for trends were obtained using the total scores of the dietary indices as continuous variables.



Abbreviations: HEI-2015 = Healthy eating Index 2015; AHEI-2010 = Alternate Healthy Eating Index 2010; aMED = Alternate Mediterranean Diet; DASH = Dietary Approaches to Stop Hypertension; HR = Hazard Ratio.

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